IN THE UNITED STATES DISTRICT COURT FOR THE MIDDLE DISTRICT OF TENNESSEE NASHVILLE DIVISION

RUTH SMITH, Individually and as Widow for the Use and Benefit of Herself and the Next of Kin of RICHARD SMITH, Deceased,	)	**Case #: 3:05-00444**
	)	**Judge Trauger**
Plaintiff,	)	
-against-	)	
PFIZER INC., PARKE-DAVIS, a division of Warner-Lambert Company and Warner-Lambert Company LLC, WARNER-LAMBERT COMPANY, WARNER-LAMBERT COMPANY LLC and JOHN DOE(S) 1-10,	)	
Defendants.	)	

PLAINTIFF'S RESPONSE TO DEFENDANTS' OBJECTIONS TO THE EXPERT WITNESS STATEMENT OF DR. CHERYL BLUME

Plaintiff, by and through her attorneys, The Lanier Law Firm, P.L.L.C. and Finkelstein & Partners, LLP, respectfully responds to Defendants' Objections to the expert witness statement of Dr. Cheryl Blume as follows.

PRELIMINARY STATEMENT

On January 31, 2008, after reviewing clinical trial data for eleven antiepileptic drugs (including Neurontin), the FDA issued an Alert "Information for Healthcare Professionals Suicidality and Antiepileptic Drugs," advising that "All patients who are currently taking or staring on an antiepileptic drug should be closely monitored for notable changes in behavior that could indicate the emergence or worsening of suicidal thoughts or behavior or depression." *See* Declaration of Kenneth B. Fromson, Ex. A. In a December 16, 2008 letter, the FDA mandated that the manufacturers of the eleven antiepileptic drugs include a package insert, **specifically**

directed to the patient, with the drug. Fromson Decl., Ex. B. The FDA specifically advised Pfizer Inc. that "based on new safety information regarding the risk of suicidal thoughts or behaviors with AEDs, a Risk Evaluation and Mitigation Strategy (RES) (including a Medication Guide) is required for Neurontin.". *Id.* Consequently, the FDA-mandated 2009 Neurontin label and patient information guide contain some of the warnings Plaintiff has advocated, and which Defendants should have provided for their drug Neurontin prior to Plaintiff's decedent's suicide. The pertinent information from the new 2009 Neurontin Label is as follows:

> **WARNINGS**
> **Suicidal Behavior and Ideation**
> Antiepileptic drugs (AEDs), including Neurontin, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Fromson Decl., Ex. C.

On April 23, 2009, the FDA advised Defendants that in "a March 17, 2009, letter we informed you that we had determined that the Medication Guide should be comprehensive and should include all risk information reflective of your labeling that is necessary for patients' safe and effective use of Neurontin." Fromson Decl., Ex. D. The Medication Guide is clearly written for the patient's benefit and safety and alerts the patient to the following adverse conditions:

What is the most important information I should know about NEURONTIN?

1. **NEURONTIN may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.**

2. **Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:**
   - thoughts about suicide or dying
   - attempts to commit suicide
   - new or worse depression
   - new or worse anxiety
   - feeling agitated or restless
   - panic attacks
   - trouble sleeping (insomnia)
   - new or worse irritability
   - acting aggressive, being angry, or violent
   - acting on dangerous impulses
   - an extreme increase in activity and talking (mania)
   - other unusual changes in behavior or mood

Fromson Decl., Ex. E. Under these special circumstances, Tennessee law regarding the learned intermediary rule, which limits a manufacturers duty to warn only to a physician, will only serve to dilute the very warnings to patients that the FDA has determined to be necessary and appropriate for the safe use of the antiepileptics, including Neurontin.

ARGUMENT

I. DR. BLUME'S OPINIONS ARE NOT CONTRARY TO TENNESSEE'S LEARNED INTERMEDIARY RULE

There have been other instances where there are special circumstances, and the courts have determined that an exception to the learned intermediary rule was appropriate, and manufacturers were found to have a duty to warn the consumers:

> (1) vaccine inoculations, see e.g., *Davis v. Wyeth Laboratories, Inc.,* 399 F.2d 121, 130-31(9th Cir. 1968) (duty of manufacturer of polio vaccine to warn consumers as to risks involved was not met by disclosures of its salesman to medical society to whom vaccine was sold, where, while the drug was denominated a prescription drug, it was not dispensed as such, but rather was

dispensed to all comers at mass clinics without an individualized balancing by a physician of the risks involved); *Reyes v. Wyeth Laboratories*, 498 F.2d 1264, 1276 (5th Cir.) (where manufacturer of prescription drug learns or has reason to know that it will not be dispensed by a physician, manufacturer must provide consumer with adequate information so that he can balance risks and benefits of given medication himself), cert. denied, 419 U.S. 1096, 42 L. Ed. 2d 688, 95 S. Ct. 687 (1974); (2) oral contraceptives, see e.g., *MacDonald v. Ortho Pharmaceutical Corp.*, 394, Mass. 131, 135-38, 475 N.E.2d 65 (manufacturer of oral contraceptives is not justified in relying on warnings to medical profession to satisfy its common-law duty to warn ultimate user of dangers inherent in their use in light of heightened participation of patients in decisions relating to use of the pill, substantial risks affiliated with use of the pill, feasibility of direct warnings by manufacturer to user, limited participation of physician who generally writes only annual prescriptions, possibility that oral communications between physician and user may be insufficient or too scanty standing alone fully to apprise user of the dangers, and fact that the product is specifically subject to extensive federal regulation), cert. denied, 474 U.S. 920, 88 L. Ed. 2d 258, 106 S. Ct. 250 (1985); *Odgers v. Ortho Pharmaceutical Corp.*, 609 F. Supp. 867, 878 (E.D. Mich. 1985) (manufacturer of oral contraceptive has duty to warn the user of the possible side effects because "patient does not rely on the physician to nearly the same degree when it comes to choosing a method of contraception as in a decision regarding a therapeutic drug"); (3) contraceptive devices, see e.g., *Hill v. Searle Laboratories*, 884 F.2d 1064, 1070-71 (8th Cir 1989) (learned intermediary rule inapplicable to manufacturer of intrauterine device because treating physician generally does not make an intervening, individualized medical judgment in the birth control decision, it was feasible to warn ultimate user, and such warning was required by FDA regulations); (4) drugs advertised directly to consumers, see e.g., *Edwards v. Basel Pharmaceuticals*, 933 P.2d 298, 303 (Okla. 1977) (manufacturer of nicotine patches not automatically shielded from liability under learned intermediary doctrine by properly warning the prescribing physician when FDA requires warnings to be given directly to patient with a prescribed drug); (5) over-promoted drugs, see e.g., *Proctor v. Davis*, 291 Ill. App. 3d 265, 682 N.E. 1203, 1214-15, 225 Ill. Dec. 127 (Ill. App. 1997) (learned intermediary doctrine does not apply where defendant manufacturer promoted and developed off-label use of prescription drug); and (6) drugs withdrawn from the market, see e.g., *Nichols v. Mc Neilab, Inc.*, 850 F. Supp. 562, 565 (E.D. Mich. 1993) (learned intermediary doctrine does not apply where prescription drug manufacturer that previously marketed its product for intermittent use withdraws its product from the wholesale market).

Vitanza v. Upjohn Co., 48 F. Supp. 2d 124, 129-30 (D. Conn. 1999)

Edwards v. Basel v. Pharmaceutical concerns a products liability case where nicotine patches were prescribed to a patient by a physician and the Supreme Court of Oklahoma

responded to a certified question from the U.S. Court of Appeals for the Tenth Circuit regarding whether the FDA's mandate that the warning be provided to users of the patches would be an exception to the learned intermediary rule. 933 P.2d 298. Fromson Decl., Ex. F. The Supreme Court of Oklahoma found such an exception to the learned intermediary rule when "the Food and Drug Administration mandates that a warning be given directly to the consumer." *Id.* at 301. In so concluding, the Supreme Court of Oklahoma stated the following:

> We hold that when the FDA requires warnings be given directly to the patient with a prescribed drug, an exception to the "learned intermediary doctrine" has occurred, and the manufacturer is not automatically shielded from liability by properly warning the prescribing physician. When this happens the manufacturer's duty to warn the consumer is not necessarily satisfied by compliance with FDA minimum warning requirements. The required warnings must not be misleading, and must be adequate to explain to the user the possible dangers associated with the product. Whether that duty has been satisfied is governed by the common law of the state, not the regulations of the FDA, and necessarily implicates a fact-finding process, something beyond our assignment in response to this certified question.

Id. at 303.

In *MacDonald v. Ortho Pharmaceutical Corp.***,** the Supreme Judicial Court of Massachusetts found that manufacturers of birth control pills presented a special situation in which the learned intermediary rule which limited defendants' liability to warning the physician did not apply, and stated that:

> the manufacturer of oral contraceptives is not justified in relying on warnings to the medical profession to satisfy its common law duty to warn, and that the manufacturer's obligation encompasses a duty to warn the ultimate user. Thus, the manufacturer's duty is to provide to the consumer written warnings conveying reasonable notice of the nature, gravity, and likelihood of known or knowable side effects, and advising the consumer to seek fuller explanation from the prescribing physician or other doctor of any such information of concern to the consumer.

394 Mass. 131, 138-39 (Mass 1985). Fromson Decl., Ex. G. In determining that defendant manufacturers were responsible to the ultimate consumer of the birth control pills, the Court

looked to the fact that the FDA had found it necessary to mandate that users of the pills be provided with specific written warnings:

> [T]he birth control pill is specifically subject to extensive Federal regulation. The FDA has promulgated regulations designed to ensure that the choice of "the pill" as a contraceptive method is informed by comprehensible warnings of potential side effects. See notes 3 and 4, *supra*. These regulations, and subsequent amendments, have their basis in the FDA commissioner's finding, after hearings, that "[b]ecause oral contraceptives are ordinarily taken electively by healthy women who have available to them alternative methods of treatment, and because of the relatively high incidence of serious illnesses associated with their use, . . . users of these drugs should, without exception, be furnished with written information telling them of the drug's benefits and risks." 43 Fed. Reg. 4215 (1978). The **FDA also found that the facts necessary to informed decisions by women as to use of oral contraceptives are "too complex to expect the patient to remember everything told her by the physician," and that, in the absence of direct written warnings, many potential users of "the pill" do not receive the needed information "in an organized, comprehensive, understandable, and handy-for-future-reference form**." 35 Fed. Reg. 9002 (1970).

Id. at 137-38 (emphasis added).

It is the law of the case that Defendants as pharmaceutical manufacturers bear a heightened duty to warn physicians and patients because they engaged in off-label marketing of a drug:

> Based on the reasoning of this caselaw, the Court concludes that a manufacturer of a pharmaceutical has a duty to disclose to **physicians and patients** material facts about the risks of the drug, <u>particularly when it is engaged in off-label marketing</u> for uses not approved by the FDA, if it knows that the plaintiff and/or his prescriber does not know or cannot reasonably discover the undisclosed facts.

See In re Neurontin Mktg., Sales Practices & Prods. Liab. Litig., 618 F. Supp. 2d 96, 110 (D. Mass. 2009) (emphasis added).

This is one of those special circumstances where the FDA has acknowledged that there are adverse mood and behavioral changes and where it is critical that patients adequately monitor these changes themselves so that they may contact a physician. Therefore, the FDA mandated that additional warnings in the form of a patient's Medication Guide, separate and in addition to

the normal labeling requirements that usually are required by the FDA for prescription medications. The Medication Guide is particularly written in lay language and addressed specifically to patients who are ingesting Neurontin.

Plaintiff submits that Defendants indeed do have a heightened duty to warn in this case, and that the FDA has made certain that this heightened duty to warn extends to the Defendants providing a warning to the patients who are prescribed and ingesting Neurontin. Defendants should not be permitted to use the learned intermediary rule to shield them from liability under the special circumstances of this case. To do so would be contrary to the law of the case, would serve to seriously dilute and undermine the authority of the FDA mandate for a Medication Guide for patients who consume Neurontin, and would only serve as incentive for the manufacturers of Neurontin, or other such drug manufacturers, not to abide by such FDA mandates to warn patients directly in the form of medication guides.

II. DR. BLUME'S WITNESS STATEMENT SUCCINCTLY SETS FORTH THE OPINIONS AND BASES FOR SAID OPINIONS AS DESCRIBED IN HER EXTENSIVE EXPERT REPORT, AND IT SHOULD NOT BE EXCLUDED FOR NOT CONTAINING EVERY ASPECT OF THE EXPERT REPORT

Defendants argue this point as if Dr. Blume's witness statement is the sum total of her opinions and their bases. This is simply not true. Dr. Blume's report and declaration provide in extraordinary detail her synthesis and interpretation of the evidence that she reviewed. It would be all but impossible for Dr. Blume to recite every basis in a succinct witness statement before the jury.

As part of her non-litigation activities, Dr. Blume is asked to opine upon conduct and whether such conduct complies with applicable regulations. She has been performing these tasks for more than 25 years. She has served as the individual required to answer to the FDA on regulatory compliance for numerous pharmaceutical companies and regularly interacts with the

FDA even today. She does nothing more in her witness statement when she makes the very same assessments as to whether Defendants' conduct complied with regulations and sound pharmacovigilance practices. These are not simple determinations and require an exhaustive review of the records, whether in the course of litigation or non-litigation activities.

III. DR. BLUME'S OPINIONS ON A HEIGHTENED DUTY TO WARN OR MONITOR ARE BASED UPON SOUND REASONING AND ARE ADMISSIBLE

The Honorable Patti B. Saris, U.S.D.J., who has presided over the Neurontin MDL since its inception, has concisely stated the following about Defendants' heightened duty to warn:

> Based on the reasoning of this caselaw, the Court concludes that a manufacturer of a pharmaceutical has a duty to disclose to **physicians and patients** material facts about the risks of the drug, particularly when it is engaged in off-label marketing for uses not approved by the FDA, if it knows that the plaintiff and/or his prescriber does not know or cannot reasonably discover the undisclosed facts.

See In re Neurontin Mktg., Sales Practices & Prods. Liab. Litig., 618 F. Supp. 2d 96, 110 (D. Mass. 2009) (emphasis added). Here, Dr. Blume's opinions are completely consistent with the law of this case.

Defendants attack Dr. Blume for not being a medical doctor. Plaintiff concedes that Dr. Blume is not a medical doctor. Defendants assert that simply because she is not a medical doctor, she is unqualified to render her opinions. However, just because Dr. Blume is not a medical doctor who treats live patients does not mean that she is unqualified to interpret the diagnoses of those who do so. In fact, Dr. Blume has been performing this very task as part of her professional, non-litigation practice for more than 25 years. She has written hundreds of package inserts, developed more than 20 New Drug Applications (NDA's), and has been responsible for the regulatory and pharmacovigilance practices for dozens of products.

Defendants clearly ignore the provisions of Fed. R. Evid. 702, which state "a witness qualified as an expert by ***knowledge***, skill, ***experience***, ***training***, or education, may testify thereto

in the form of an opinion or otherwise ..." For more than 25 years, Dr. Blume has worked in the pharmaceutical industry rendering the very opinions that Defendants claim she is unqualified to make. At no point do Defendants demonstrate that Dr. Blume is actually providing a diagnosis for a given patient. Furthermore, Defendants provide no credible evidence that Dr. Blume must be a medical doctor to render her opinions.

The MDL court reviewed this very issue with respect to Dr. Blume and found in its *Daubert* decision that she was competent to testify to the extent that she is working with information regularly used by the FDA and industry professionals.

As to the concept of a vulnerable subpopulation, Defendants' experts themselves raise this issue when they assert throughout their expert disclosures *ad nauseum* that certain populations of Neurontin users are more susceptible to suicidal behavior (e.g., because of chronic pain, disease, and even old age). It is absurd for Defendants to argue that Dr. Blume's opinions that there are vulnerable populations are unfounded when their own experts, as well as Defendants internally argue the same thing.

Since both sides agree that there are individuals who are at a greater risk of suicide and suicidal adverse events, Dr. Blume is well within her province to discuss how the company should have responded to such information.

IV. DR. BLUME DOES NOT RENDER OPINIONS ON SUBSEQUENT REMEDIAL MEASURES

Defendants' own objection is fatal to their claim that Dr. Blume is testifying to a purportedly inadmissible subsequent remedial measure. They cite to Dr. Blume’s statement: “My point in showing you this document is that Defendants should have and could have come up with this plan years before Mr. Smith died.” (Def. Mem, Docket No. 232, at p.10).

On its face, the statement does not assert that Defendants are negligent because they took the action in question after Mr. Smith died. Rather, the statement asserts that it was feasible for such actions to take place and that Defendants should have taken the action earlier than they did. Defendants ignore the portion of Dr. Blume's statement that says Defendants *should* have taken the actions. This is not the same as feasibility and is a point with which Defendants and their experts disagree.

Therefore, because Dr. Blume's statement goes not only to the feasibility but to the necessity of the actions, the testimony is admissible as evidence of negligence. Moreover this Court already ruled in regard to the FDA mandated measures that:

> Here, the FDA mandated that Pfizer add the warnings. The policy behind Rule 407 is not implicated, so it does not bar admission of the 2009 label and patient guide. *Rozier v. Ford Motor Co.*, 573 F.2d 1332, 1343 (5th Cir. 1978) (declining to apply Rule 407 because "the remedial measure was to be required in any event by a superior authority, the National Highway Traffic Safety Administration"); *Lolie v. Ohio Brass Co.*, 502 F.2d 741, 744 (7th Cir. 1974) (admitting evidence that a state mine inspector ordered a mine operator to add support to a power cable after an accident). Because evidence of the FDA's regulatory actions and the 2009 label and patient guide are relevant and not otherwise barred, the defendants' motion will be denied.

Docket No. 199.

V. DR. BLUME IS QUALIFIED TO RENDER OPINIONS ON NEURONTIN'S MECHANISM OF ACTION

This issue was resolved squarely by the MDL court in its *Daubert* opinion (MDL Docket No. 1775) where Judge Saris found that Dr. Blume's opinions met the standards of *Daubert* :

> Defendants contend that, despite her industry experience, Dr. Blume is not qualified to testify about Neurontin's mechanism of action or any medical theory of causation. In offering an opinion on general causation, Dr. Blume does discuss mechanism of action and biological plausibility, yet her report and testimony overwhelmingly focus on the review and evaluation of adverse events associated with Neurontin. In performing this review, Dr. Blume states that she used the same methods that she employs when preparing a drug development for submission to the FDA. (Blume Decl. ¶ 5.) She states that she reviewed the same

> types of records and applied the same analytical methods used by the FDA to evaluate a drug's risks, benefits, safety, and efficacy. (Blume Decl. ¶ 9.)
>
> Dr. Blume is amply qualified at least to evaluate the adverse event data and other sources of information regularly used by the FDA and industry professionals.

Dr. Blume is a pharmacologist and reviewed hundreds of thousands of pages of Neurontin related materials, far more than any of Defendants' experts. She uses the mechanism of action of Neurontin in the context of house such information should have been used in a regulatory context. Defendants' suggestion that simply because Dr. Blume is not going to be the expert who provides detailed opinions on the mechanisms of action of Neurontin means she is not qualified to discuss that information in the context of regulatory requirements is wrong. Indeed, Defendants' own expert witnesses will all be testifying to various aspects of the FDA alert, despite Dr. Robert Gibbons providing the detailed review.

VI. DR. BLUME'S OPINIONS BASED IN PART ON DATA PROVIDED WITH ASSISTANCE OF PLAINTIFF'S COUNSEL SHOULD NOT BE EXCLUDED

This Court has already addressed the issue as to expert's reliance on charts prepared by Plaintiffs' counsel in denying Defendants' motion *in limine* concerning Dr. Charles King. (Motion, Docket No. 118; Ruling, Docket No. 200.) Plaintiff' incorporates their opposition (Docket No. 164) as the issues are essentially the same as those presented here. Plaintiff believes that the Court's ruling for Dr. King is directly applicable to Dr. Blume. In fact, this issue was squarely rejected by Judge Saris in MDL 1629.

Next, Defendants' suggestion that Dr. Blume's opinions were not disclosed are patently absurd. In particular, Defendants seek to preclude exhibits disclosed as long ago as 2008 as part of the *Daubert* record; indeed, Defendants do not dispute they have possessed Dr. Blume's opinions and these exhibits since 2008. These exhibits were prepared in response to Defendants'

challenge to Dr. Blume's testimony on general causation. Dr. Blume submitted a Declaration that referenced the Declaration of Keith Altman that was also prepared as part of Plaintiff's opposition. During the June 2008 Daubert hearing, Dr. Blume was extensively cross-examined on her opinions, including her Declaration. More importantly, Defendants' experts, Dr. Sheila Weiss Smith, Dr. Alex Ruggieri, and Dr. Janet Arrowsmith-Lowe specifically reviewed both Declarations and rendered opinions in November 2008. It is nonsensical for Defendants to argue that the contents of these Declarations have not been adequately disclosed. In fact, many of the charts from Dr. Weiss Smith's proposed testimony were created in specific response to Dr. Blume's Declaration.

CONCLUSION

In view of the above, Plaintiff respectfully requests that this Court reject Defendants' Objections concerning the expert witness statement of Dr. Cheryl Blume.

Dated: May 13, 2010

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this the 13th day of May, 2010, I electronically filed the foregoing document with the Clerk of the Court, United States District Court for the Middle District of Tennessee, using the CM/ECF system. True and correct copies of the foregoing documents are being served via the Court's CM/ECF system on the following:

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